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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/808,706	03/14/2001	William A. McMillan	22660-0025 DIV 2	6375

7590 07/23/2004

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EXAMINER	
SWITZER, JULIET CAROLINE	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 07/23/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/808,706	MCMILLAN ET AL.	
	Examiner	Art Unit	
	Juliet C. Switzer	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 May 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *52-79* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *64-79* is/are allowed.

6)☒ Claim(s) *52-54 and 56-63* is/are rejected.

7)☒ Claim(s) *55* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is written in response to applicant's correspondence that was received 5/21/04. Applicant amended cancelled all pending claims and added new claims 52-79. Claims 52-79 are pending and examined herein.

2. This action is **FINAL**.

3. The objection to the abstract is moot in view of the amended abstract.

Claim Rejections - 35 USC § 112

4. The previously set forth rejection under 112 1st paragraph is moot in view of applicant's cancellation of the rejected claims. The new claims do not contain the subject matter that was at issue in the withdrawn rejections.

5. Likewise, the rejections under 112 2nd paragraph are moot in view of the cancellation of the claims.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 52, 53, 54, 56-63 are rejected under 35 U.S.C. 102(e) as being anticipated by Wittwer *et al.* (US 6303305).

Wittwer *et al.* teach a method for determining an unknown starting quantity of a target nucleic acid sequence in a test sample, the method comprising the steps of:

(a) amplifying the unknown starting quantity of the target nucleic acid sequence in the test sample (Col. 4, lines 13-16; Col. 7, lines 47-48);

(b) amplifying a plurality of known starting quantities of a calibration nucleic acid sequence in respective calibration samples (Col. 7, lines 48-50);

(c) determining a respective threshold value for each of the known starting quantities of the calibration nucleic acid sequence in the calibration samples and for the target nucleic acid sequence in the test sample, wherein the threshold value is determined for each nucleic acid sequence in a respective sample by:

(i) measuring at a plurality of times during amplification, at least one signal whose intensity is related to the quantity of the nucleic acid sequence being amplified in the sample (Col. 7, lines 48-50) ;

(ii) storing signal values defining a growth curve for the nucleic acid sequence (Col. 7, line 51; Figure 2A);

(iii) calculating a derivative growth curve (Col. 7, lines 51-53);

(iv) identifying a positive peak of the derivative (Col. 7, lines 51-52; Col. 5, lines 62-65);

(v) determining if the positive peak exceeds a threshold level; and

(vi) if the positive peak exceeds the threshold level, then calculating a threshold value (i.e. a cycle number) associated with the positive of the derivative (Col. 5, lines 43-67; Col. 7, lines 54-55);

(d) deriving a calibration curve from the threshold values determined for the known starting quantities of the calibration nucleic acid sequence in the calibration samples (Col. 7, lines 44-56); and

(e) determining the starting quantity of the target nucleic acid sequence in the test sample using the calibration curve and the threshold value determined for the target sequence (Col. 7, lines 55-56).

With respect to parts (c)(v) and (c)(vi) of claim 52, Wittwer *et al.* are inherently practice these steps in the actual determination of a positive peak since the determination of a positive peak itself requires that the point which is determined to be the peak surpasses threshold values which are each of the other points on the curve. Thus, Wittwer *et al.* determine that the point designated as the maximum (positive peak) exceeds a number of user defined thresholds which are defined as all of the other data points in the second derivative curve. After determining that the positive peak exceeds these threshold levels, then Wittwer *et al.* calculate a threshold value associated with the positive peak of the derivative.

With regard to claim 53, Wittwer *et al.* teach a threshold value that comprises cycle number, that is, Wittwer *et al.* teach that that the determination of extrema, such as the maximum or minimum of the second derivative of the curve provides a set point for the definition of the fractional cycle number characteristic for each value, which reflects the initial concentration of the analyte (Col. 5, lines 62-67). That is, the threshold amount of cycles (i.e. time necessary) for a given concentration of sample to produce an observable signal.

With regard to claim 54, Wittwer *et al.* the determination of cycle number is a determination of the elapsed time of amplification, as each cycle of a PCR amplification is a

fixed period of time (see for example lines 25-30 of Col. 8) and thus, cycle number is a measure of the time elapsed from the beginning of the PCR.

With regard to claim 56, the threshold level is considered a user-defined threshold level as the user determines that the identification will be of a maximum of the derivative, thus inherently determining that the threshold will be a point on the derivative that is above all other points on the derivative curve.

With regard to claim 57, Wittwer *et al.* teach a step of calculating a derivative of the growth curve that comprises calculating a second derivative of the growth curve, wherein the characteristic comprises a positive peak of the second derivative, referred to therein as the maxima of the derivative (Col. 5, lines 62-65).

With regard to claim 58, Wittwer *et al.* teach a step of calculating a first derivative of the growth curve wherein the characteristic comprises a postitive peak of the first derivative (Col. 5, lines 62-65).

With regard to claim 59, Wittwer *et al.* disclose the method wherein the calculation comprises calculating second derivative values of the growth curve at a number of different measurement points in the reaction to yield a plurality of second derivative data points derivative data points, the characteristic comprising a positive peak of the second derivative, and the step of determining the threshold value associated with the positive peak comprising fitting a second order curve to the data point and calculating the threshold value as the location of a peak of the second order curve (Col. 6, lines 1-34, Figure 4).

With regard to claim 52, Wittwer *et al.* teach a step of determining the second derivative of the growth curve with respect to cycle number and calculating the threshold cycle number as

the location, in cycles, of a maximum of the second derivative (Col. 5, lines 62-65; Figure 2; Example 1(B)). With regard to claim 61, Wittwer *et al.* additionally teach the use of the maximum of the first derivative (Col. 5, lines 62-65).

With regard to claim 62, Wittwer *et al.* teach a step of determining the second derivative of the growth curve with respect to cycle number (which is a measure of time of amplification) and calculating the threshold cycle number as the location, in cycles, of a maximum of the second derivative (Col. 5, lines 62-65; Figure 2; Example 1(B)). With regard to claim 63, Wittwer *et al.* additionally teach the use of the maximum of the first derivative (Col. 5, lines 62-65).

Response to Remarks

Applicant's remarks regarding independent claim 52 are addressed in the new grounds of rejection applied to the newly added claims. Namely, the feature which applicants assert is missing from the disclosure of Wittwer *et al.* is in fact inherent to the method practiced by Wittwer *et al.*

Conclusion

8. Claims 64-79 are allowed. Wittwer *et al.* does not teach or suggest a method wherein it is determined if the signal value defining the growth curve at the zero crossing or the negative peak of the second derivative of the growth curve exceeds a threshold level.

9. Claim 55 objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Wittwer *et al.* do not teach or suggest a method of claim 52 wherein the threshold level is a noise-based threshold level.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Juliet C Switzer whose telephone number is (571) 272-0753. The examiner can normally be reached on Monday through Friday, from 9:00 AM until 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached by calling (571) 272-0782.

The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)272-0507.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the

USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Juliet C. Switzer
Examiner
Art Unit 1634

July 14, 2004